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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	DEC 01	ChemPort single article sales feature unavailable
NEWS 3	APR 03	CAS coverage of exemplified prophetic substances enhanced
NEWS 4	APR 07	STN is raising the limits on saved answers
NEWS 5	APR 24	CA/CAplus now has more comprehensive patent assignee information
NEWS 6	APR 26	USPATFULL and USPAT2 enhanced with patent assignment/reassignment information
NEWS 7	APR 28	CAS patent authority coverage expanded
NEWS 8	APR 28	ENCOMPLIT/ENCOMPLIT2 search fields enhanced
NEWS 9	APR 28	Limits doubled for structure searching in CAS REGISTRY
NEWS 10	MAY 08	STN Express, Version 8.4, now available
NEWS 11	MAY 11	STN on the Web enhanced
NEWS 12	MAY 11	BEILSTEIN substance information now available on STN Easy
NEWS 13	MAY 14	DGENE, PCTGEN and USGENE enhanced with increased limits for exact sequence match searches and introduction of free HIT display format
NEWS 14	MAY 15	INPADOCDB and INPAFAMDB enhanced with Chinese legal status data
NEWS 15	MAY 28	CAS databases on STN enhanced with NANO super role in records back to 1992
NEWS 16	JUN 01	CAS REGISTRY Source of Registration (SR) searching enhanced on STN
NEWS 17	JUN 26	NUTRACEUT and PHARMAML no longer updated
NEWS 18	JUN 29	IMSCOPROFILE now reloaded monthly
NEWS 19	JUN 29	EPFULL adds Simultaneous Left and Right Truncation (SLART) to AB, MCLM, and TI fields
NEWS 20	JUL 09	PATDPAFULL adds Simultaneous Left and Right Truncation (SLART) to AB, CLM, MCLM, and TI fields

NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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FILE 'HOME' ENTERED AT 12:05:32 ON 09 JUL 2009

=> file reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 1.10 1.10

FILE 'REGISTRY' ENTERED AT 12:08:43 ON 09 JUL 2009
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DICTIONARY FILE UPDATES: 8 JUL 2009 HIGHEST RN 1161500-61-3

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http://www.cas.org/support/stngen/stndoc/properties.html

=> s dipeptidyl () dipeptidase () IV and DPP-IV
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 26.75 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
822 DIPEPTIDYL
1243 DIPEPTIDASE
13665 IV
65 IVS
13730 IV
(IV OR IVS)
0 DIPEPTIDYL (W) DIPEPTIDASE (W) IV
206 DPP
2 DPPS
208 DPP

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```
                (DPP OR DPPS)
         13665 IV
            65 IVS
         13730 IV
                (IV OR IVS)
             6 DPP-IV
                (DPP(W)IV)
L1           0 DIPEPTIDYL (W) DIPEPTIDASE (W) IV AND DPP-IV

=> file hcaplus
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                  27.23      28.33

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FILE COVERS 1907 - 9 Jul 2009  VOL 151 ISS 2
FILE LAST UPDATED: 8 Jul 2009  (20090708/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Apr 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Apr 2009

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the second quarter of 2009.

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This file contains CAS Registry Numbers for easy and accurate
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=> s dipeptidyl () dipeptidase () IV and DPP-IV
          5572 DIPEPTIDYL
          2548 DIPEPTIDASE
           462 DIPEPTIDASES
          2676 DIPEPTIDASE
                (DIPEPTIDASE OR DIPEPTIDASES)
        559207 IV
          1143 IVS
        560238 IV
                (IV OR IVS)
            16 DIPEPTIDYL (W) DIPEPTIDASE (W) IV
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          5214 DPP
           242 DPPS
          5420 DPP
                 (DPP OR DPPS)
        559207 IV
          1143 IVS
        560238 IV
                 (IV OR IVS)
          1285 DPP-IV
                 (DPP(W)IV)
L2           4 DIPEPTIDYL (W) DIPEPTIDASE (W) IV AND DPP-IV

=> s DPP-IV
          5214 DPP
           242 DPPS
          5420 DPP
                 (DPP OR DPPS)
        559207 IV
          1143 IVS
        560238 IV
                 (IV OR IVS)
L3        1285 DPP-IV
                 (DPP(W)IV)

=> s l3 and () Inhibit?
MISSING TERM 'AND (W'
The search profile that was entered contains a logical
operator followed immediately by another operator.

=> s l3 () inhibit?
       2157778 INHIBIT?
L4         593 L3 (W) INHIBIT?

=> s l4 and diabet?
        181423 DIABET?
L5         482 L4 AND DIABET?

=> s l5 and review/dt
       2278038 REVIEW/DT
L6         101 L5 AND REVIEW/DT

=> s l6 and pyrid?
        412646 PYRID?
L7           0 L6 AND PYRID?

=> s l6 and pyridine
        233855 PYRIDINE
         16709 PYRIDINES
        238720 PYRIDINE
                 (PYRIDINE OR PYRIDINES)
L8           0 L6 AND PYRIDINE

=> s l6 and pd < november 2003
      23933259 PD < NOVEMBER 2003
                 (PD<20031100)
L9           9 L6 AND PD < NOVEMBER 2003
```

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=> d l9, ibib abs hitstr, 1-9
THE ESTIMATED COST FOR THIS REQUEST IS 50.76 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L9 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:859022 HCAPLUS
DOCUMENT NUMBER: 140:139599
TITLE: Enhancing incretin action for the treatment of type 2 diabetes
AUTHOR(S): Drucker, Daniel J.
CORPORATE SOURCE: Banting and Best Diabetes Centre, Department of Medicine, Toronto General Hospital, University of Toronto, ON, Can.
SOURCE: Diabetes Care (2003), 26(10), 2929-2940
CODEN: DICAD2; ISSN: 0149-5992
PUBLISHER: American Diabetes Association, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Studies were carried out to examine the mechanisms of action, therapeutic potential, and challenges inherent in the use of incretin peptides and dipeptidyl peptidase-IV (DPP-IV) inhibitors for the treatment of type 2 diabetes. The scientific literature describing the biol. importance of incretin peptides and DPP-IV inhibitors in the control of glucose homeostasis has been reviewed, with an emphasis on mechanisms of action, exptl. diabetes, human physiol. expts., and short-term clin. studies in normal and diabetic human subjects. Glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) exert important effects on β-cells to stimulate glucose-dependent insulin secretion. Both peptides also regulate β-cell proliferation and cytoprotection. GLP-1, but not GIP, inhibits gastric emptying, glucagon secretion, and food intake. The glucose-lowering actions of GLP-1, but not GIP, are preserved in subjects with type 2 diabetes. However, native GLP-1 is rapidly degraded by DPP-IV after parenteral administration; hence, degradation-resistant, long-acting GLP-1 receptor (GLP-1R) agonists are preferable agents for the chronic treatment of human diabetes. Alternatively, inhibition of DPP-IV-mediated incretin degradation represents a complementary therapeutic approach, as orally available DPP-IV inhibitors have been shown to lower glucose in exptl. diabetic models and human subjects with type 2 diabetes. Thus, GLP-1R agonists and DPP-IV inhibitors have shown promising results in clin. trials for the treatment of type 2 diabetes. The need for daily injections of potentially immunogenic GLP-1-derived peptides and the potential for unanticipated side effects with chronic use of DPP-IV inhibitors will require ongoing scrutiny of the risk-benefit ratio for these new therapies as they are evaluated in the clinic.
REFERENCE COUNT: 172 THERE ARE 172 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:601213 HCAPLUS
DOCUMENT NUMBER: 140:195191

Updated Search

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TITLE: Dipeptidyl-peptidase IV from bench to bedside: an update on structural properties, functions, and clinical aspects of the enzyme DPP IV
AUTHOR(S): Lambeir, Anne-Marie; Durinx, Christine; Scharpe, Simon; De Meester, Ingrid
CORPORATE SOURCE: Laboratory of Medical Biochemistry, University of Antwerp, Wilrijk, Belg.
SOURCE: Critical Reviews in Clinical Laboratory Sciences (2003), 40(3), 209-294
CODEN: CRCLBH; ISSN: 1040-8363
PUBLISHER: CRC Press LLC
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Dipeptidyl-peptidase IV/CD26 (DPP IV) is a cell-surface protease belonging to the prolyloligopeptidase family. It selectively removes the N-terminal dipeptide from peptides with proline or alanine in the second position. Apart from its catalytic activity, it interacts with several proteins, for instance, adenosine deaminase, the HIV gp120 protein, fibronectin, collagen, the chemokine receptor CXCR4, and the tyrosine phosphatase CD45. DPP IV is expressed on a specific set of T lymphocytes, where it is up-regulated after activation. It is also expressed in a variety of tissues, primarily on endothelial and epithelial cells. A soluble form is present in plasma and other body fluids. DPP IV has been proposed as a diagnostic or prognostic marker for various tumors, hematol. malignancies, immunol., inflammatory, psychoneuroendocrine disorders, and viral infections. DPP IV truncates many bioactive peptides of medical importance. It plays a role in glucose homeostasis through proteolytic inactivation of the incretins. DPP IV inhibitors improve glucose tolerance and pancreatic islet cell function in animal models of type 2 diabetes and in diabetic patients. The role of DPP IV/CD26 within the immune system is a combination of its exopeptidase activity and its interactions with different mols. This enables DPP IV/CD26 to serve as a co-stimulatory mol. to influence T cell activity and to modulate chemotaxis. DPP IV is also implicated in HIV-1 entry, malignant transformation, and tumor invasion.
REFERENCE COUNT: 526 THERE ARE 526 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:496268 HCAPLUS
DOCUMENT NUMBER: 140:23327
TITLE: Neutral endopeptidase 24.11 and dipeptidyl peptidase IV are both involved in regulating the metabolic stability of glucagon-like peptide-1 in vivo
AUTHOR(S): Plamboeck, Astrid; Holst, Jens J.; Carr, Richard D.; Deacon, Carolyn F.
CORPORATE SOURCE: Department of Medical Physiology, Panum Institute, Copenhagen, DK-2200, Den.
SOURCE: Advances in Experimental Medicine and Biology (2003), 524(Dipeptidyl Aminopeptidases in Health and Disease), 303-312
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal; General Review

Updated Search

STNupdated

LANGUAGE: English
AB A review discusses recent studies examining the physiol. role of dipeptidyl peptidase IV (DPP IV) and neutral endopeptidase 24.11 (NEP 24.11) in regulating the metabolic stability of glucagon-like peptide-1 (GLP-1) in vivo. DPP IV inhibition protects intact GLP-1 from N-terminal truncation, leading to improved insulinotropic and anti-hyperglycemic activity. NEP 24.11 inhibition also contributes to improving the metabolic stability of GLP-1 in vivo. Combined NEP 24.11 and DPP IV inhibition is superior to DPP IV inhibition alone in reducing clearance and improving the anti-hyperglycemic and insulinotropic activity of GLP-1, providing the first evidence that NEP 24.11 inhibition may also have therapeutic potential in diabetes treatment.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:496262 HCAPLUS
DOCUMENT NUMBER: 139:224543
TITLE: Implementation of GLP-1 based therapy of type 2 diabetes mellitus using DPP-IV inhibitors
AUTHOR(S): Holst, Jens Juul
CORPORATE SOURCE: Department of Medical Physiology, University of Copenhagen, The Panum Institute, Copenhagen, DK-2200, Den.
SOURCE: Advances in Experimental Medicine and Biology (2003), 524(Dipeptidyl Aminopeptidases in Health and Disease), 263-279
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. GLP-1 is a peptide hormone from intestinal mucosa. It is secreted in response to meal ingestion and normally functions in the so-called ileal brake i.e. inhibition of upper gastrointestinal motility and secretion when nutrients are present in the distal small intestine. It also induces satiety and promotes tissue deposition of ingested glucose by stimulating insulin secretion. In addition, the hormone has been demonstrated to promote insulin biosynthesis and insulin gene expression and to have trophic effects on beta cells. The trophic effects include proliferation of existing beta cells, maturation of new cells from duct progenitor cells and inhibition of apoptosis. Furthermore glucagon secretion is inhibited. Because of these effects, the hormone effectively improves metabolism in patients with type 2 diabetes mellitus. However, continuous administration of the peptide is necessary because of an exceptionally rapid degradation catalyzed by dipeptidyl peptidase IV. With inhibitors of this enzyme, it is possible to protect the endogenous hormone and thereby elevate both fasting and postprandial levels of the active hormone. This leads to enhanced insulin secretion and glucose turnover. But whether DPP-IV inhibition enhances all effects of the endogenous peptide remain a question. The mode of GLP-1 action is complex involving also interactions with sensory.
REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Updated Search

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L9 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:329929 HCAPLUS
DOCUMENT NUMBER: 139:172966
TITLE: Dipeptidyl peptidase IV inhibitors as new therapeutic agents for the treatment of type 2 diabetes
AUTHOR(S): Augustyns, Koen; Van der Veken, Pieter; Senten, Kristel; Haemers, Achiel
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Antwerp, Antwerpen, B-2610, Belg.
SOURCE: Expert Opinion on Therapeutic Patents (2003), 13(4), 499-510
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Type 2 diabetes is the most prevalent form of diabetes. Incretion hormones play an important role in normal and pathol. blood glucose homeostasis. The role of dipeptidyl peptidase IV (DPP IV) in the inactivation of glucagon-like peptide-1 (GLP-1), one of the most important incretins, is well-established. Therefore, DPP IV inhibitors are investigated as new therapeutic agents for the treatment of Type 2 diabetes. A summary of DPP IV inhibitors reported until 1998 and a more extensive discussion of more recent inhibitors found in literature and patent applications will be provided. The therapeutic potential of several aminoacyl pyrrolidides, aminoacyl thiazolidides and aminoacyl pyrrolidine-2-nitriles will be reviewed.
REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:158145 HCAPLUS
DOCUMENT NUMBER: 139:239392
TITLE: Dipeptidyl peptidase IV inhibitors
AUTHOR(S): Evans, D. Michael
CORPORATE SOURCE: Department of Medicinal Chemistry, Ferring Research Limited, Southampton, SO16 7NP, UK
SOURCE: IDrugs (2002), 5(6), 577-585
CODEN: IDRUFN; ISSN: 1369-7056
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The patent literature for dipeptidyl peptidase IV (DPP-IV) inhibitors for the period of Jan. 2001 to May 2002 is reviewed. There has been increased interest in DPP-IV inhibitors since their potential for the treatment of diabetes was identified. This review will focus on reversible inhibitors of the enzyme, for which the primary interest has been for use in the treatment of Type II diabetes. The majority of the new chemical entities reported are dipeptide-like inhibitors that mimic the preferred substrates and the best of these display nanomolar activity. There have been fewer reports of non-peptide inhibitors suggesting that it is much more difficult to identify new classes of inhibitors. In addition to new chemical entities this review will cover new indications for DPP-IV inhibitors that have been identified using previously reported inhibitors as research tools.

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REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:8969 HCAPLUS
DOCUMENT NUMBER: 139:130
TITLE: Therapeutic potential of dipeptidyl peptidase IV inhibitors for the treatment of type 2 diabetes
AUTHOR(S): Drucker, Daniel J.
CORPORATE SOURCE: Banting and Best Diabetes Centre, Toronto General Hospital, Toronto, ON, M5G 2C4, Can.
SOURCE: Expert Opinion on Investigational Drugs (2003), 12(1), 87-100
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Incretins are peptide hormones, exemplified by glucose-dependent insulinotropic peptide and glucagon-like peptide 1 that are released from the gut in response to nutrient ingestion and enhance glucose-stimulated insulin secretion. Incretin action is terminated due to N-terminal cleavage of the peptides by the aminopeptidase dipeptidyl peptidase IV (DPP-IV). Hence, inhibition of glucose-dependent insulinotropic peptide and glucagon-like peptide 1 degradation via reduction of DPP-IV activity represents an innovative strategy for enhancing incretin action in vivo. This review summarizes the biol. of incretin action, the structure, expression and pleiotropic biol. activities of DPP-IV and provides an overview of the rationale, potential merits and theor. pitfalls in the development of DPP-IV inhibitors for the treatment of type 2 diabetes.
REFERENCE COUNT: 159 THERE ARE 159 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:704165 HCAPLUS
DOCUMENT NUMBER: 132:45051
TITLE: Dipeptidyl-peptidase IV (CD26)-role in the inactivation of regulatory peptides
AUTHOR(S): Mentlein, R.
CORPORATE SOURCE: Anatomisches Institut der Universitat Kiel, Kiel, D-24098, Germany
SOURCE: Regulatory Peptides (1999), 85(1), 9-24
CODEN: REPPDY; ISSN: 0167-0115
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 112 refs. Dipeptidyl-peptidase IV (DPP IV/CD26) has a dual function as a regulatory protease and as a binding protein. Its role in the inactivation of bioactive peptides was recognized 20 yr ago due to its unique ability to liberate Xaa-Pro or Xaa-Ala dipeptides from the N-terminus of regulatory peptides, but further examples are now emerging from in vitro and vivo expts. Despite the minimal N-terminal truncation by DPP IV, many mammalian regulatory peptides are inactivated - either totally or only differentially - for certain receptor subtypes. Important

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DPP IV substrates include neuropeptides like neuropeptide Y or endomorphin, circulating peptide hormones like peptide YY, growth hormone-releasing hormone, glucagon-like peptides(GLP)-1 and -2, gastric inhibitory polypeptide as well as paracrine chemokines like RANTES (regulated on activation normal T cell expressed and secreted), stromal cell-derived factor, eotaxin and macrophage-derived chemokine. Based on these findings the potential clin. uses of selective DPP IV inhibitors or DPP IV-resistant analogs, especially for the insulinotropic hormone GLP-1, have been tested to enhance insulin secretion and to improve glucose tolerance in diabetic animals. Thus, DPP IV appears to be a major physiol. regulator for some regulatory peptides, neuropeptides, circulating hormones and chemokines.

REFERENCE COUNT: 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:699999 HCAPLUS
DOCUMENT NUMBER: 130:60497
TITLE: Perspectives in Diabetes: inhibition of the activity of dipeptidyl-peptidase IV as a treatment for type 2 diabetes
AUTHOR(S): Holst, Jens J.; Deacon, Carolyn F.
CORPORATE SOURCE: Department of Medical Physiology, University of Copenhagen, Copenhagen, DK-2200, Den.
SOURCE: Diabetes (1998), 47(11), 1663-1670
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 82 refs. The insulinotropic hormone, glucagon-like peptide 1 (GLP-1), which has been proposed as a new treatment for type 2 diabetes, is metabolized extremely rapidly by the ubiquitous enzyme, dipeptidyl peptidase IV (DPP-IV), resulting in the formation of a metabolite, which may act as an antagonist at the GLP-1 receptor. Because of this, the effects of single injections of GLP-1 are short-lasting, and for full demonstration of its antidiabetogenic effects, continuous i.v. infusion is required. To exploit the therapeutic potential of GLP-1 clin., we here propose the use of specific inhibitors of DPP-IV. We have demonstrated that the administration of such inhibitors may completely protect exogenous GLP-1 from DPP-IV-mediated degradation, thereby greatly enhancing its insulinotropic effect, and provided evidence that endogenous GLP-1 may be equally protected. Preliminary studies by others in glucose-intolerant exptl. animals have shown that DPP-IV inhibition greatly ameliorates the condition. GLP-1 has multifaceted actions, which include stimulation of insulin gene expression, trophic effects on the β-cells, inhibition of glucagon secretion, promotion of satiety, inhibition of food intake, and slowing of gastric emptying, all of which contribute to normalizing elevated glucose levels. Because of this, we predict that inhibition of DPP-IV, which will elevate the levels of active GLP-1 and reduce the levels of the antagonistic metabolite, may be useful to treat impaired glucose tolerance and perhaps prevent transition to type 2 diabetes. The actions of DPP-IV, other than degradation of GLP-1, particularly in the immune system are discussed, but it is concluded that side effects of inhibition therapy are likely to be mild. Thus, DPP-IV

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inhibition may be an effective supplement to diet and exercise treatment in attempts to prevent the deterioration of glucose metabolism associated with the Western lifestyle.
REFERENCE COUNT: 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 12:05:32 ON 09 JUL 2009)

FILE 'REGISTRY' ENTERED AT 12:08:43 ON 09 JUL 2009
L1 0 S DIPEPTIDYL () DIPEPTIDASE () IV AND DPP-IV

FILE 'HCAPLUS' ENTERED AT 12:09:07 ON 09 JUL 2009
L2 4 S DIPEPTIDYL () DIPEPTIDASE () IV AND DPP-IV
L3 1285 S DPP-IV
L4 593 S L3 () INHIBIT?
L5 482 S L4 AND DIABET?
L6 101 S L5 AND REVIEW/DT
L7 0 S L6 AND PYRID?
L8 0 S L6 AND PYRIDINE
L9 9 S L6 AND PD < NOVEMBER 2003

=> s l4 and obesity
58572 OBESITY
88 OBESITIES
58575 OBESITY
(OBESITY OR OBESITIES)
L10 166 L4 AND OBESITY

=> s l10 and review/dt
2278038 REVIEW/DT
L11 6 L10 AND REVIEW/DT

=> s l11 not l9
L12 6 L11 NOT L9

=> d l12, ibib abs hitstr, 1-6
THE ESTIMATED COST FOR THIS REQUEST IS 33.84 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L12 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2009:150093 HCAPLUS
TITLE: GLP-1 analogues, DDP-IV inhibitors and the metabolic syndrome
AUTHOR(S): Stonehouse, A. H.; Holcombe, J. H.; Kendall, D. M.
CORPORATE SOURCE: Medical Affairs Scientist, Amylin Pharmaceuticals, Inc., San Diego, CA, USA
SOURCE: Therapeutic Strategies in Metabolic Syndrome (2008), 137-157. Editor(s): Fonseca, Vivian. Clinical Publishing: Oxford, UK.
CODEN: 69LIPT; ISBN: 978-1-904392-99-6
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB The metabolic syndrome and type 2 diabetes are metabolic disorders that

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remain inextricably intertwined. The emergence of obesity, type 2 diabetes, and CV disease as significant clin. and public health concerns in both the developed and developing worlds has further increased the awareness of the metabolic syndrome as a potential target for treatment in hopes of reducing the future risk of both progression of hyperglycemia and CV events in this population. The improved identification and treatment of individuals with the metabolic syndrome will require therapies that possess myriad effects on all components of the syndrome. Therapies for hyperglycemia (including metformin, TZDs, and the incretin mimetics) have demonstrated a broad array of potentially favorable effects. Currently, the cardiometabolic risk factors, including obesity, glucose intolerance, dyslipidemia and hypertension, identified by IDF as critical components of the metabolic syndrome, are only treated either individually or targeted with compds. that specifically target weight loss. Most anti-diabetes agents improve glycemic control but are hampered by their association with body weight gain. The availability of the incretin mimetic exenatide, and potentially other incretin-based therapies, along with the DPP-IV inhibitors, represent a hopeful and novel approach to the treatment of type 2 diabetes. Most notably, the incretin mimetics (currently represented by exenatide) offer the hope for sustained improvement in glycemic control with progressive reduction in body weight, both very valuable characteristics, particularly for the type 2 diabetes patient with the metabolic syndrome. Whether these effects on glucose and body weight will also be seen in those with the metabolic syndrome in the absence of type 2 diabetes is not currently known. However, the reduction in body weight with concomitant improvement in cardiometabolic risk factors in patients treated with exenatide may have a potentially beneficial role for treatment of the metabolic syndrome in the years ahead. Further study in this population will obviously be required before such an approach to therapy can be advocated for individuals without a diagnosis of type 2 diabetes.

REFERENCE COUNT: 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:617794 HCAPLUS
DOCUMENT NUMBER: 149:69266
TITLE: The obesity epidemic: pharmacological challenges
AUTHOR(S): Bloom, Stephen R.; Kuhajda, Francis P.; Laher, Ismail; Pi-Sunyer, Xavier; Ronnett, Gabriele V.; Tan, Tricia M. M.; Weigle, David S.
CORPORATE SOURCE: Hammersmith Hospital, Imperial College, London, W12 0NN, UK
SOURCE: Molecular Interventions (2008), 8(2), 82-98
CODEN: MIONAR; ISSN: 1534-0384
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. As obesity claims an increasing number of lives every year, our collective awareness of obesity as a global epidemic has heightened. There are complex origins for this relentless epidemic: easy access to large quantities of inexpensive foods that are calorie-rich; eating habits that have changed to match fast-paced and

automated lifestyles; and increasingly sedentary work and recreation. These factors compound inherited tendencies to store excess calories as a defense mechanism for times of famine-the so-called thrifty-gene theory. It is estimated that more than thirty percent of adults, and about fifteen percent of juveniles, are obese. These statistics are accompanied by dramatic increases of diseases such as type 2 diabetes, cardiovascular and respiratory diseases, depression, and some forms of cancer. More than 300,000 obesity-related deaths occur in the US yearly; in fact, the incidence of type 2 diabetes in children has increased by more than tenfold. The urgency of the obesity epidemic has fueled biomedical research into the mechanisms that underlie energy homeostasis and the perturbations of metabolic balances that result in disease. Many of these mechanisms-both peripheral and within the central nervous system-suggest promising avenues for pharmacol. intervention into obesity, overweight, and the comorbidities of modern, globalized living.

REFERENCE COUNT: 174 THERE ARE 174 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1349377 HCAPLUS
DOCUMENT NUMBER: 148:327916
TITLE: Type 2 diabetes mellitus: epidemiology, pathophysiology, unmet needs and therapeutical perspectives
AUTHOR(S): Virally, M.; Blickle, J.-F.; Girard, J.; Halimi, S.; Simon, D.; Guillausseau, P.-J.
CORPORATE SOURCE: Service de Medecine B, APHP, Hopital Lariboisiere, Universite Denis-Diderot-Paris-VII, Paris, 75010, Fr.
SOURCE: Diabetes & Metabolism (2007), 33(4), 231-244
CODEN: DIMEFW; ISSN: 1262-3636
PUBLISHER: Elsevier Masson SAS
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. In France, prevalence of drug-treated diabetes reached 3.60% in 2005, with 92% of type 2 diabetic patients. In 2007, there are probably nearly 3 000 000 diagnosed or undiagnosed diabetic patients. Ageing of the population and increase in obesity are the main causes of this "diabetes epidemic". Type 2 diabetes is a multifactorial disease, defined as resulting from defects in insulin secretion (including abnormalities in pulsatility and kinetics, quant. and qual. abnormalities of insulin, β-cell loss progressing with time) associated with insulin resistance (affecting liver, and skeletal muscle) and increased glucagon secretion. The lack of compensation of insulin resistance by augmented insulin secretion results in rise in blood glucose. To achieve satisfactory glycemic control in order to prevent diabetes related complications, drug therapy is generally required in addition to life style changes. Currently available oral therapies offer a large panel of complementary drugs, but they have several contraindications and side effects. In spite of major advances in the management of type 2 diabetes, and the strictness of new guidelines, some goals remain unachieved and the new family of insulin-secretors (DPP-IV inhibitors, GLP-1 analogs) should enrich therapeutic approaches.

REFERENCE COUNT: 125 THERE ARE 125 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

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FORMAT

L12 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:639144 HCAPLUS
DOCUMENT NUMBER: 147:225904
TITLE: Emerging therapies for type 2 diabetes
AUTHOR(S): Stonehouse, Anthony H.; Maggs, David G.
CORPORATE SOURCE: Amylin Pharmaceuticals, Inc., San Diego, CA, USA
SOURCE: Current Drug Therapy (2007), 2(2), 151-160
CODEN: CDTUBV; ISSN: 1574-8855
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Type 2 diabetes results from progressive β-cell dysfunction and insulin resistance, leading to progressive worsening of glycemic control, and increased risk of microvascular and macrovascular complications. Traditionally, treatment strategies for type 2 diabetes have concentrated on compensating for insulin deficiency and reducing insulin resistance. These approaches sequentially utilize diet and exercise, oral antidiabetic drug therapy, and ultimately, exogenous insulin. However, current therapies have little effect on the inexorable decline of β-cell dysfunction, and in a group of patients already overweight or obese, treatment often comes with further weight gain. Consequently, patients often experience deterioration of glycemic control as their disease progresses while battling obesity. Several new therapies including new insulin platforms and new classes of pharmaceutical agents with unique modes of action have recently been introduced or are in clin. development for use in patients with type 2 diabetes. These include amylinomimetics, incretin mimetics, DPP -IV inhibitors, and glucagon antagonists. These new agents improve glycemia and in some instances can reduce body weight Furthermore, anti-obesity agents, either currently available or in development, are being investigated for their potential to treat diabetes. This review focuses primarily on these new therapeutic approaches, particularly those that improve glycemic control while improving control of body weight
REFERENCE COUNT: 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:546228 HCAPLUS
DOCUMENT NUMBER: 145:353786
TITLE: Dipeptidyl peptidase IV/CD26: structure-function, regulation of metabolism and T-cells
AUTHOR(S): Lenhard, James M.; Malhotra, Rajneesh
CORPORATE SOURCE: Department of Metabolic Diseases, GlaxoSmithKline Inc., Research Triangle Park, NC, USA
SOURCE: Focus on Diabetes Mellitus Research (2006), 199-224. Editor(s): Ford, Ashley M. Nova Science Publishers, Inc.: Hauppauge, N. Y.
CODEN: 69IEHS; ISBN: 1-59454-225-2
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review. Dipeptidyl Peptidase-IV (DPP-IV or CD26) is a membrane bound and secreted serine protease constitutively expressed by a variety of

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cells, including kidney, liver and activated T-cells. DPP-IV modulates the activity of several peptides involved in nutritional control (e.g., the PACAP/glucagon family), immunomodulation (e.g., chemokines) and mood (e.g., neuropeptides). The incretins, GLP-1 and GIP, are inactivated by DPP-IV resulting in decreased glucose-induced insulin secretion. The crystal structure of DPP-IV reveals substrate and inhibitor binding involves the α/-hydrolase and eight-bladed -propeller domains. Oral DPP-IV inhibitors stabilize the incretins, which regulate islet -cell growth and enhance insulin secretion and glucose disposal. Unlike sulfonylureas, DPP-IV inhibitors increase glucose-induced insulin secretion and do not cause fasting hypoglycemia. Rodents deficient in DPP-IV are healthy with improved glucose tolerance and insulin sensitivity, reduced susceptibility to obesity, and altered T-cell dependent antigen specific antibody production and cytokine secretion. Chronic treatment of diabetic rodents and humans with DPP-IV inhibitors improves insulin sensitivity and decreases serum glucose and lipid levels. It is also reported that DPP-IV inhibitors are involved in immunomodulation by regulating chemokine activity and T-cell activation by a neg. co-stimulatory signal. Altered signaling by the incretins, cytokines and other peptides may contribute to the metabolic effects of DPP-IV inhibitors.

REFERENCE COUNT: 148 THERE ARE 148 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:571490 HCAPLUS
DOCUMENT NUMBER: 144:192453
TITLE: MK-0431 : agent for type 2 diabetes and dipeptidyl-peptidase IV (CD26) inhibitor
AUTHOR(S): Sorbera, L. A.; Castaner, J.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2005), 30(4), 337-343
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The incretin hormone glucagon-like peptide-1 (GLP-1, GLP-1[7-36]amide) plays a crucial role in the regulation of insulin by acting on the pancreas to potentiate glucose-induced insulin secretion. GLP-1 also beneficially slows gastric emptying, reduces appetite and restores β-cell function, and has been the subject of research efforts to develop agents for the treatment of type 2 diabetes. However, GLP-1 has an extremely short half-life and is not suitable for therapeutic use. It is rapidly hydrolyzed by the circulating enzyme dipeptidyl-peptidase IV (DPP-IV), which cleaves the mol. at the N-terminal, giving rise to the inactive truncated fragment GLP-1(9-36)amide. On the other hand, administration of a DPP-IV inhibitor could enhance the half-life of GLP-1 and could therefore produce the same pleiotropic effects as exogenously administered GLP-1 or GLP-1 analogs. Thus, one of the newer targets for the treatment of diabetes is the serine protease DPP-IV. MK-0431 (Ono-5435) is a novel, potent, orally active β-amino acid-derived DPP-IV inhibitor that has exhibited good pharmacokinetics in mice, rats, dogs and monkeys and was chosen for

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further development as a treatment for type 2 diabetes. It has been shown to be effective in insulin-resistant mice and mice with diet-induced obesity, and was safe and effective in patients with type 2 diabetes. The agent has reached phase III development as a treatment for this condition.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 12:05:32 ON 09 JUL 2009)

FILE 'REGISTRY' ENTERED AT 12:08:43 ON 09 JUL 2009
L1 0 S DIPEPTIDYL () DIPEPTIDASE () IV AND DPP-IV

FILE 'HCAPLUS' ENTERED AT 12:09:07 ON 09 JUL 2009
L2 4 S DIPEPTIDYL () DIPEPTIDASE () IV AND DPP-IV
L3 1285 S DPP-IV
L4 593 S L3 () INHIBIT?
L5 482 S L4 AND DIABET?
L6 101 S L5 AND REVIEW/DT
L7 0 S L6 AND PYRID?
L8 0 S L6 AND PYRIDINE
L9 9 S L6 AND PD < NOVEMBER 2003
L10 166 S L4 AND OBESITY
L11 6 S L10 AND REVIEW/DT
L12 6 S L11 NOT L9

=> s l4 and glucose () tolerance
479940 GLUCOSE
925 GLUCOSES
480160 GLUCOSE
(GLUCOSE OR GLUCOSES)
135275 TOLERANCE
9890 TOLERANCES
141456 TOLERANCE
(TOLERANCE OR TOLERANCES)
17169 GLUCOSE (W) TOLERANCE
L13 88 L4 AND GLUCOSE (W) TOLERANCE

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2278038 REVIEW/DT
L14 14 L13 AND REVIEW/DT

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L15 13 L14 NOT L12

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THE ESTIMATED COST FOR THIS REQUEST IS 73.32 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L15 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2009:105647 HCAPLUS
DOCUMENT NUMBER: 151:23607
TITLE: Saxagliptin, a dipeptidyl peptidase IV inhibitor for

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the treatment of type 2 diabetes
AUTHOR(S): Gallwitz, Baptist
CORPORATE SOURCE: Department of Medicine IV, Eberhard-Karls-University, Tuebingen, 72076, Germany
SOURCE: IDrugs (2008), 11(12), 906-917
CODEN: IDRUFN; ISSN: 1369-7056
PUBLISHER: Thomson Reuters
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Saxagliptin, a dipeptidyl peptidase-IV (DPP-IV) inhibitor, is currently under development by Bristol-Myers Squibb Co, AstraZeneca plc and Otsuka Pharmaceutical Co Ltd for the treatment of type 2 diabetes. The compound has high selectivity for DPP-IV compared with other dipeptidyl peptidases and a duration profile designed for once-daily dosing. DPP-IV inhibitors act by increasing levels of glucagon-like peptide-1, which stimulates insulin secretion. In animal studies, saxagliptin improved glucose clearance and raised insulin levels in rodents. Clin. trials have demonstrated a dose-dependent inhibition of DPP-IV by saxagliptin without serious side effects. Results have demonstrated that treatment with saxagliptin lowers blood glucose levels, with good tolerability and safety. The specific advantages of saxagliptin over other DPP-IV inhibitors may lie in its long-lived, effective and highly specific inhibition of DPP-IV, making once-daily treatment feasible, effective and safe.
REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1283601 HCAPLUS
DOCUMENT NUMBER: 149:485900
TITLE: Glucagon like peptide-1 modulators as newer target for diabetes
AUTHOR(S): Vaidya, H. B.; Goyal, R. K.
CORPORATE SOURCE: Department of Pharmacology, L.M. College of Pharmacy, Navrangpura, Ahmedabad, 380009, India
SOURCE: Current Drug Targets (2008), 9(10), 911-920
CODEN: CDTUAU; ISSN: 1389-4501
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Diabetes mellitus (DM) has been recognized as a growing world-wide epidemic by many health advocacy groups including the World Health Organization (WHO). DM affects about 6% of the North American population. A recent report estimated that 8.2% of adult population worldwide has impaired glucose tolerance. Current treatment approaches include diet, exercise, and a variety of pharmacol. agents including insulin, biguanides, sulfonylureas and thiazolidinediones. New therapies are still needed to control metabolic abnormalities, and also to preserve β-cell mass and to prevent loss of β-cell function. In many cases monotherapy gradually fails to improve blood glucose control and combination therapy is employed. The long-term success of these treatments varies substantially. Thus, there is an imperative need for novel therapeutic approaches for glycemic control that can complement existing therapies and possibly attempt to preserve normal physiol. response to meal intake. Glucagon-like peptide 1 (GLP-1) is a drug

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candidate which potentially fulfills these conditions. Glucoregulatory actions of GLP-1 include glucose-dependent enhancement of insulin secretion, inhibition of glucagon secretion, slowing of gastric emptying and reduction of food intake. GLP-1 is rapidly inactivated by the amino peptidase, dipeptidyl peptidase-IV (DPP-IV), and the utility of DPP-IV inhibitors are also under investigation. There is a recent upsurge in the development of GLP-1 mimetics and DPP-IV inhibitors as potential antidiabetic agents. The present review summarizes the concepts of GLP-1 based therapy for type 2 diabetes and the current preclin. and clin. development in GLP-1 modulators.

REFERENCE COUNT: 135 THERE ARE 135 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1052708 HCAPLUS
DOCUMENT NUMBER: 150:256491
TITLE: Postprandial hyperglycemia
AUTHOR(S): Raghavan, Vasudevan A.; Garber, Alan J.
CORPORATE SOURCE: Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, Ohio State University, Columbus, OH, USA
SOURCE: Type 2 Diabetes Mellitus (2008), 97-113. Editor(s): Feinglos, Mark N.; Bethel, M. Angelyn. Humana Press Inc.: Totowa, N. J.
CODEN: 69KYYD; ISBN: 978-1-58829-794-5
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review. In healthy individuals, blood glucose levels in the fasting state are maintained by basal insulin secretion. After a meal, the rise in postprandial glucose (PPG) is controlled by the rapid release of insulin, stimulated by both glucose and the intestinal production of incretin hormones. In diabetic individuals, postprandial insulin secretion is insufficient, resulting in postprandial hyperglycemia (PPHG). Sustained hyperglycemia results in "glucotoxicity," that results in progressively irreversible β-cell dysfunction. There is increasing evidence that PPHG exerts a more deleterious effect on endothelial function and the vascular system, than elevation of fasting plasma glucose (FPG). In particular, individuals with normal FPG but impaired glucose tolerance (IGT) have significantly increased risk of cardiovascular events. With the recognition of the importance of PPHG and the availability of new pharmacol. options, management of diabetes will shift to greater attention to PPG levels. Currently, there are many approaches to tackle PPHG; dietary management and promotion of exercise are very effective. In particular, meglitinides, disaccharidase inhibitors, sulfonylureas and short acting insulin analogs are particularly suited to treat PPHG. The development of glucagon-like peptide 1 (GLP-1) agonists such as exendin and dipeptidyl peptidase IV (DPP-IV) inhibitors such as vildagliptin holds great promise as addnl. agents in achieving stringent control of PPG. There is an urgent need for the conduct of randomized controlled trials with long term follow-up, and these studies ought to be powered to study the effect of a variety of therapeutic agents that modify PPG levels, on multiple morbidity endpoints and mortality, in individuals with prediabetes, T1DM and T2 DM. Until such data is available, routine

monitoring of PPG levels with a view to impact diabetic outcomes cannot be recommended.
REFERENCE COUNT: 105 THERE ARE 105 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:832392 HCAPLUS
DOCUMENT NUMBER: 149:282381
TITLE: Significance of postprandial hyperglycemia and pharmacotherapy
AUTHOR(S): Mizutani, Masakazu; Yamada, Nobuhiro
CORPORATE SOURCE: Kozawa Eye Hospital and Diabetes Center, Japan
SOURCE: Rinsho Eiyo (2008), 113(1), 19-26
CODEN: RNEYAW; ISSN: 0485-1412
PUBLISHER: Ishiyaku Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review on the impaired glucose tolerance as a risk factor of cardiovascular disease; the reference value of postprandial glucose; pathogenesis and clin. importance of postprandial hyperglycemia; influence of diets on postprandial glucose levels; amelioration of postprandial hyperglycemia by α-glucosidase inhibitors, glinides, and fast-acting insulin analogs; and novel drugs (GLP-1 analogs and DPP-IV inhibitors).

L15 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:321833 HCAPLUS
DOCUMENT NUMBER: 148:298892
TITLE: Anti-diabetes effects of K579, dipeptidyl peptidase IV inhibitor
AUTHOR(S): Takasaki, Kotaro
CORPORATE SOURCE: Fac. Pharm. Sci., Fukuoka University, Fukuoka, 814-0180, Japan
SOURCE: Fukuoka Daigaku Yakugaku Shuho (2008), 8, 13-24
CODEN: FDYSAE; ISSN: 1346-1559
PUBLISHER: Fukuoka Daigaku Kenkyu Suishinbu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. Dipeptidyl peptidase IV (DPP-IV) inhibitors are expected to be categorized in a new type of antidiabetic drugs. K579 is a long-acting DPP-IV inhibitor. In Wistar rats, K579 suppressed the blood glucose elevation after an oral glucose tolerance test with the increment of plasma insulin and active forms of glucagon-like peptide-1. During repetitive glucose loading using Zucker fatty rats, pretreatment with K579 attenuated the glucose excursion after the second glucose loading as well as the first glucose loading without inducing hypoglycemia. The kinetic study using cell extract revealed that K579 was a more potent and slower binding inhibitor than the existing DPP-IV inhibitor (NVP-DPP728). Next, the plasma concns. of K579 after oral administration to rats were measured. However, K579 was eliminated rapidly from plasma after oral administration to rats. Therefore, it was postulated that there are active metabolites of K579 in rat plasma. The duration of inhibitory action of plasma DPP-IV after the administration of K579 in bile duct-cannulated rats was shorter than that

in sham-operated rats. The bile collected from K579-treated rats exhibited tardive and potent inhibitory activity of normal rat plasma. Finally, the effects of orally administered DPP-IV inhibitor on the glucose-lowering effect of glibenclamide were investigated. Treatment with K579 inhibited the plasma DPP-IV activity even 8 h after the administration. K579 significantly suppressed the blood glucose elevation in glibenclamide-pretreated rats without excessive hypoglycemia. These results suggest that K579 sustained the duration of inhibitory action of plasma DPP-IV by the character as a slow-binding inhibitor, and, as well, by the presence of metabolites of K579 which exhibit the inhibitory activity of DPP-IV. These profiles of K579 might be advantageous over the existing DPP-IV inhibitor with respect to less dosing frequency, and could be useful agent to correct the postprandial glucose excursion in type 2 diabetes patients by combination treatment with glibenclamide.

L15 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:164336 HCAPLUS
DOCUMENT NUMBER: 148:416929
TITLE: Dipeptidyl peptidase IV inhibitors and diabetes therapy
AUTHOR(S): McIntosh, Christopher H. S.
CORPORATE SOURCE: Diabetes Research Group and Department of Cellular and Physiological Sciences, Life Sciences Institute, The University of British Columbia, Vancouver, BC, Can.
SOURCE: Frontiers in Bioscience (2008), 13, 1753-1773
CODEN: FRBIF6; ISSN: 1093-4715
URL: http://www.bioscience.org/asp/getfile.asp?FileName=/2008/v13/af/2797/2797.pdf
PUBLISHER: Frontiers in Bioscience
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Current type 2 diabetes therapies are mainly targeted at stimulating pancreatic beta-cell secretion and reducing insulin resistance. A number of alternative therapies are currently being developed to take advantage of the actions of the incretin hormones Glucagon-Like Peptide-1 (GLP-1) and Glucose-dependent Insulinotropic Polypeptide (GIP). These hormones are released from the small intestine in response to nutrient ingestion and stimulate insulin secretion in a glucose-dependent manner. One approach to potentiating their actions is based on inhibiting dipeptidyl peptidase IV (DPP IV), the major enzyme responsible for degrading the incretins in vivo. DPP IV exhibits characteristics that have allowed the development of specific orally administered inhibitors with proven efficacy in improving glucose tolerance in animal models of diabetes. A number of clin. trials have demonstrated that DPP IV inhibitors are effective in improving glucose disposal and reducing Hb Alc levels in type 2 diabetic patients and one inhibitor, sitagliptin, is now in therapeutic use, with others likely to receive FDA approval in the near future. Studies aimed at elucidating the mode of action of the inhibitors are still ongoing. Both enhancement of insulin secretion and reduction in glucagon secretion, resulting from the blockade of incretin degradation, are believed to play important roles in DPP IV inhibitor action. Preclin. studies indicate that increased levels of incretins improve beta-cell secretory function and exert effects on beta-cell mitogenesis

and survival that can preserve beta-cell mass. Roles for other hormones, neuropeptides and cytokines in DPP IV inhibitor-medicated responses are also possible.
REFERENCE COUNT: 278 THERE ARE 278 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:633823 HCAPLUS
DOCUMENT NUMBER: 147:202847
TITLE: DPP IV inhibitors - current evidence and future directions
AUTHOR(S): Vilsboell, Tina; Knop, Filip K.
CORPORATE SOURCE: Department of Internal Medicine F, Gentofte Hospital, University of Copenhagen, Hellerup, DK-2900, Den.
SOURCE: British Journal of Diabetes & Vascular Disease (2007), 7(2), 69-74
CODEN: BJDVAI; ISSN: 1474-6514
PUBLISHER: MediNews (Diabetes) Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are responsible for the higher insulin response after oral vs. i.v. glucose administration. This effect is called the incretin effect. An impaired incretin effect in patients with type 2 diabetes focused attention on the possible importance of GIP and GLP-1 in diabetes mellitus. Metabolic control can be markedly improved by administration of exogenous GLP-1, but the native peptide is almost immediately degraded by the enzyme dipeptidyl peptidase IV (DPP IV) and, therefore, has little clin. value. Orally active inhibitors of DPP IV have now been developed and have been shown to enhance endogenous levels of GLP-1, resulting in improved glucose tolerance, lasting improvement of HbA1C and improved beta-cell function. In general the DPP IV inhibitors are weight neutral, and well tolerated. One DPP IV inhibitor, sitagliptin, was approved as a once-daily oral therapy for the treatment of type 2 diabetes mellitus in Mexico and USA in 2006, and Europe in 2007. Other DPP IV inhibitors are in late-stage clin. development.
REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:553805 HCAPLUS
DOCUMENT NUMBER: 146:474632
TITLE: Dipeptidyl peptidase IV inhibitors: the next generation of new promising therapies for the management of type 2 diabetes
AUTHOR(S): Sebokova, Elena; Christ, Andreas D.; Boehringer, Markus; Mizrahi, Jacques
CORPORATE SOURCE: Vascular and Metabolic Diseases, F. Hoffmann-La Roche Ltd., Basel, 4070, Switz.
SOURCE: Current Topics in Medicinal Chemistry (Sharjah, United Arab Emirates) (2007), 7(6), 547-555
CODEN: CTMCCL; ISSN: 1568-0266
PUBLISHER: Bentham Science Publishers Ltd.

STNupdated

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Type 2 diabetes is a chronic metabolic disease characterized by the presence of both fasting and postprandial hyperglycemia which is a result of pancreas β-cell dysfunction, deficiency in insulin secretion, insulin resistance and/or increased hepatic glucose production More recently, the role of other glucoregulatory hormones, including glucagon, amylin, and the gut peptide glucagon-like peptide (GLP)-1, and an increase in the rate of postmeal carbohydrate absorption have also been included as important pathophysiol. defects. Existing anti-diabetes medications are often unefficient at achieving sustained glycemic control because they predominantly address only a single underlying defect. A number of alternative therapies for type 2 diabetes are currently under development that take advantage of the actions of the incretin hormones glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide on the pancreatic β-cell. One such approach is based on the inhibition of dipeptidyl peptidase IV (DPP-IV), the major enzyme responsible for degrading the incretins in vivo. DPP-IV exhibits characteristics that have allowed the development of specific inhibitors with proven efficacy in improving glucose tolerance in animal models of diabetes and type 2 diabetic patients. While enhancement of insulin secretion, resulting from blockade of incretin degradation, has been proposed to be the major mode of inhibitor action, there is also evidence that inhibition of gastric emptying, reduction in glucagon secretion, peripheral insulin sensitization and important effects on β-cell differentiation and survival can potentially preserve β-cell mass, and improve insulin secretory function and glucose handling in diabetic patients. The present article focuses on the preclin. and clin. data of DPP-IV inhibitors that make it unique therapeutic agents representing the next generation of antidiabetes drugs.
REFERENCE COUNT: 107 THERE ARE 107 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:100219 HCAPLUS
DOCUMENT NUMBER: 142:232219
TITLE: Therapeutic assessment of glucagon-like peptide-1 agonists compared with dipeptidyl peptidase IV inhibitors as potential antidiabetic drugs
AUTHOR(S): Mentlein, Rolf
CORPORATE SOURCE: University of Kiel, Anatomisches Institut, Kiel, Germany
SOURCE: Expert Opinion on Investigational Drugs (2005), 14(1), 57-64
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The most prevalent form of diabetes is non-insulin-dependent or Type 2 diabetes. Innovative strategies to enhance insulin secretion and thereby improve glucose tolerance in patients with this type of diabetes are currently under preclin. and clin. investigation. These therapies include the applications of incretin hormones; gut hormones released postprandially that stimulate insulin secretion in pancreatic β-cells. Because incretin actions are

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rapidly terminated by N-terminal cleavage of these peptide hormones by the amino-peptidase dipeptidyl peptidase IV (DPP IV, CD26), the utility of DPP IV inhibitors for the treatment of Type 2 diabetes is also under investigation. This review compares the therapeutic potential and possible side effects of metabolically stable analogs/peptide agonists of the incretin glucagon-like peptide-1 (GLP-1) with the application of DPP IV inhibitors that reduce the rate of endogenous degradation of GLP-1 and other incretins. GLP-1 analogs were shown to be highly efficacious in the treatment of Type 2 diabetes, with minimal side effects. Of particular importance is the fact that they do not induce hypoglycemia. However, they are currently available only in an injectable form. In contrast, DPP IV inhibitors have the clear advantage of oral application resulting in better patient compliance. Furthermore, they also potentiate the actions of other incretins normally degraded by the action of DPP IV. However, they possess more potential side effects. Taken together, both approaches offer promising new drugs for the treatment of Type 2 diabetes.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:690503 HCAPLUS
DOCUMENT NUMBER: 141:235455
TITLE: Inhibitors of dipeptidyl peptidase IV: a novel approach for the prevention and treatment of Type 2 diabetes?
AUTHOR(S): Deacon, Carolyn F.; Ahren, Bo; Holst, Jens J.
CORPORATE SOURCE: Panum Institute, Department of Medical Physiology, University of Copenhagen, Copenhagen, DK-2200, Den.
SOURCE: Expert Opinion on Investigational Drugs (2004), 13(9), 1091-1102
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Inhibitors of the enzyme dipeptidyl peptidase IV (DPP IV) are of increasing interest to both diabetologists and the pharmaceutical industry alike, as they may become established as the next member of the oral antidiabetic class of therapeutic agents, designed to lower blood glucose and, possibly, prevent the progressive impairment of glucose metabolism in patients with impaired glucose tolerance and Type 2 diabetes. DPP IV has become a focus of attention for drug design, as it has a pivotal role in the rapid degradation of at least two of the hormones released during food ingestion, a property that has warranted the design of inhibitor-based drugs. At the mol. level, DPP IV cleaves two amino acids from the N-terminus of the intact, biol. active forms of both so-called incretin hormones, glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide (formerly known as gastric inhibitory polypeptide), resulting in truncated metabolites, which are largely inactive. Inhibition of the enzyme, therefore, is thought to increase levels of the active forms of both incretin hormones, culminating in an increase in insulin release after a meal, in a fully glucose-dependent manner. DPP IV inhibitors combine several features of interest to the drug design process. They can be readily optimized for their target and be designed as low mol. weight, orally active

entities compatible with once-daily administration.
REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:601213 HCAPLUS
DOCUMENT NUMBER: 140:195191
TITLE: Dipeptidyl-peptidase IV from bench to bedside: an update on structural properties, functions, and clinical aspects of the enzyme DPP IV
AUTHOR(S): Lambeir, Anne-Marie; Durinx, Christine; Scharpe, Simon; De Meester, Ingrid
CORPORATE SOURCE: Laboratory of Medical Biochemistry, University of Antwerp, Wilrijk, Belg.
SOURCE: Critical Reviews in Clinical Laboratory Sciences (2003), 40(3), 209-294
CODEN: CRCLBH; ISSN: 1040-8363
PUBLISHER: CRC Press LLC
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Dipeptidyl-peptidase IV/CD26 (DPP IV) is a cell-surface protease belonging to the prolyloligopeptidase family. It selectively removes the N-terminal dipeptide from peptides with proline or alanine in the second position. Apart from its catalytic activity, it interacts with several proteins, for instance, adenosine deaminase, the HIV gp120 protein, fibronectin, collagen, the chemokine receptor CXCR4, and the tyrosine phosphatase CD45. DPP IV is expressed on a specific set of T lymphocytes, where it is up-regulated after activation. It is also expressed in a variety of tissues, primarily on endothelial and epithelial cells. A soluble form is present in plasma and other body fluids. DPP IV has been proposed as a diagnostic or prognostic marker for various tumors, hematol. malignancies, immunol., inflammatory, psychoneuroendocrine disorders, and viral infections. DPP IV truncates many bioactive peptides of medical importance. It plays a role in glucose homeostasis through proteolytic inactivation of the incretins. DPP IV inhibitors improve glucose tolerance and pancreatic islet cell function in animal models of type 2 diabetes and in diabetic patients. The role of DPP IV/CD26 within the immune system is a combination of its exopeptidase activity and its interactions with different mols. This enables DPP IV/CD26 to serve as a co-stimulatory mol. to influence T cell activity and to modulate chemotaxis. DPP IV is also implicated in HIV-1 entry, malignant transformation, and tumor invasion.
REFERENCE COUNT: 526 THERE ARE 526 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:704165 HCAPLUS
DOCUMENT NUMBER: 132:45051
TITLE: Dipeptidyl-peptidase IV (CD26)-role in the inactivation of regulatory peptides
AUTHOR(S): Mentlein, R.
CORPORATE SOURCE: Anatomisches Institut der Universitat Kiel, Kiel, D-24098, Germany
SOURCE: Regulatory Peptides (1999), 85(1), 9-24

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CODEN: REPPDY; ISSN: 0167-0115
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 112 refs. Dipeptidyl-peptidase IV (DPP IV/CD26) has a dual function as a regulatory protease and as a binding protein. Its role in the inactivation of bioactive peptides was recognized 20 yr ago due to its unique ability to liberate Xaa-Pro or Xaa-Ala dipeptides from the N-terminus of regulatory peptides, but further examples are now emerging from in vitro and vivo expts. Despite the minimal N-terminal truncation by DPP IV, many mammalian regulatory peptides are inactivated - either totally or only differentially - for certain receptor subtypes. Important DPP IV substrates include neuropeptides like neuropeptide Y or endomorphin, circulating peptide hormones like peptide YY, growth hormone-releasing hormone, glucagon-like peptides(GLP)-1 and -2, gastric inhibitory polypeptide as well as paracrine chemokines like RANTES (regulated on activation normal T cell expressed and secreted), stromal cell-derived factor, eotaxin and macrophage-derived chemokine. Based on these findings the potential clin. uses of selective DPP IV inhibitors or DPP IV-resistant analogs, especially for the insulinotropic hormone GLP-1, have been tested to enhance insulin secretion and to improve glucose tolerance in diabetic animals. Thus, DPP IV appears to be a major physiol. regulator for some regulatory peptides, neuropeptides, circulating hormones and chemokines.
REFERENCE COUNT: 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:699999 HCAPLUS
DOCUMENT NUMBER: 130:60497
TITLE: Perspectives in Diabetes: inhibition of the activity of dipeptidyl-peptidase IV as a treatment for type 2 diabetes
AUTHOR(S): Holst, Jens J.; Deacon, Carolyn F.
CORPORATE SOURCE: Department of Medical Physiology, University of Copenhagen, Copenhagen, DK-2200, Den.
SOURCE: Diabetes (1998), 47(11), 1663-1670
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 82 refs. The insulinotropic hormone, glucagon-like peptide 1 (GLP-1), which has been proposed as a new treatment for type 2 diabetes, is metabolized extremely rapidly by the ubiquitous enzyme, dipeptidyl peptidase IV (DPP-IV), resulting in the formation of a metabolite, which may act as an antagonist at the GLP-1 receptor. Because of this, the effects of single injections of GLP-1 are short-lasting, and for full demonstration of its antidiabetogenic effects, continuous i.v. infusion is required. To exploit the therapeutic potential of GLP-1 clin., we here propose the use of specific inhibitors of DPP-IV. We have demonstrated that the administration of such inhibitors may completely protect exogenous GLP-1 from DPP-IV-mediated degradation, thereby greatly enhancing its insulinotropic effect, and provided evidence that endogenous GLP-1 may be equally protected. Preliminary studies by others in glucose-intolerant exptl. animals have shown that DPP-IV

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inhibition greatly ameliorates the condition. GLP-1 has multifaceted actions, which include stimulation of insulin gene expression, trophic effects on the β-cells, inhibition of glucagon secretion, promotion of satiety, inhibition of food intake, and slowing of gastric emptying, all of which contribute to normalizing elevated glucose levels. Because of this, we predict that inhibition of DPP-IV, which will elevate the levels of active GLP-1 and reduce the levels of the antagonistic metabolite, may be useful to treat impaired glucose tolerance and perhaps prevent transition to type 2 diabetes. The actions of DPP-IV, other than degradation of GLP-1, particularly in the immune system are discussed, but it is concluded that side effects of inhibition therapy are likely to be mild. Thus, DPP-IV inhibition may be an effective supplement to diet and exercise treatment in attempts to prevent the deterioration of glucose metabolism associated with the Western lifestyle.

REFERENCE COUNT: 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT